Severe nonexertional hyperthermia (classic heat stroke) in adults

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INTRODUCTION — Hyperthermia is defined as elevation of core body temperature above the normal diurnal range of 36 to 37.5ºC due to failure of thermoregulation. Hyperthermia is not synonymous with the more common sign of fever, which is induced by cytokine activation during inflammation and regulated at the level of the hypothalamus. A temperature above 40ºC (or 104ºF) is generally considered to be consistent with severe hyperthermia.

The evaluation of severe hyperthermia in adults and the management of nonexertional heat stroke will be reviewed here. Exertional heat illness (including exertional heat stroke), fever in adults, malignant hyperthermia, and neuroleptic malignant syndrome are discussed in detail separately. (See "Exertional heat illness in adolescents and adults: Epidemiology, thermoregulation, risk factors, and diagnosis" and "Exertional heat illness in adolescents and adults: Management and prevention" and "Pathophysiology and treatment of fever in adults" and "Malignant hyperthermia: Clinical diagnosis and management of acute crisis" and "Neuroleptic malignant syndrome".)

PATHOPHYSIOLOGY — Body temperature is maintained within a narrow range by balancing heat load with heat dissipation [1,2]. The body's heat load results from both metabolic processes and absorption of heat from the environment. As core temperature rises, the preoptic nucleus of the anterior hypothalamus stimulates efferent fibers of the autonomic nervous system to produce sweating and cutaneous vasodilation.

Evaporation is the principal mechanism of heat loss in a hot environment, but this becomes ineffective above a relative humidity of 75 percent [3]. The other major methods of heat dissipation—radiation (emission of infrared electromagnetic energy), conduction (direct transfer of heat to an adjacent, cooler object), and convection (direct transfer of heat to convective air currents)—cannot efficiently transfer heat when environmental temperature exceeds skin temperature. The normal regulation of body temperature is discussed separately. (See "Exertional heat illness in adolescents and adults: Epidemiology, thermoregulation, risk factors, and diagnosis", section on 'Thermoregulation in the heat'.)

Temperature elevation is accompanied by an increase in oxygen consumption and metabolic rate, resulting in hyperpnea and tachycardia. Above 42ºC (108ºF), oxidative phosphorylation becomes uncoupled, and a variety of enzymes cease to function. A cytokine-mediated systemic inflammatory response develops, and production of heat-shock proteins is increased. Blood is shunted from the splanchnic circulation to the skin and muscles, resulting in gastrointestinal ischemia and increased permeability of the intestinal mucosa. Hepatocytes, vascular endothelium, and neural tissue are most sensitive to increased core temperatures, but all organs may ultimately be involved. In severe cases, patients develop multi-organ system failure and disseminated intravascular coagulation (DIC) [2,4,5].

A number of the physiologic mechanisms for coping with an increased environmental heat load are impaired in elder patients. This includes reduced ability to deliver heat to the skin, reduced epidermal area available for heat transfer, and impaired vasodilation of the skin. These and other related problems are described in detail separately. (See "Normal aging".)

DEFINITIONS AND CLINICAL FINDINGS — Heat stroke is defined as a core body temperature usually in excess of 40ºC (104ºF) with associated central nervous system dysfunction in the setting of a large environmental heat load that cannot be dissipated [2,3,6].

There are two types of heat stroke:

- **Classic (nonexertional) heat stroke** – Classic heat stroke affects individuals (most often patients over 70 years) with underlying chronic medical conditions that impair thermoregulation, prevent removal from a hot environment, or interfere with access to hydration or attempts at cooling [7]. These conditions include cardiovascular disease, neurologic or psychiatric disorders, obesity, anhidrosis, physical disability, extremes of age, and the use of recreational drugs, such as alcohol or cocaine, and certain prescription drugs, such as beta-blockers, diuretics, or anticholinergic agents [2,8-10].

  As an example of a medication-related episode, classic heat stroke was recently reported in 60-year-old male who presented with altered mental status and a temperature of 41.9°C in the context of long-term clozapine use [11].

- **Exertional heat stroke** – Exertional heat stroke generally occurs in young, otherwise healthy individuals who engage in heavy exercise during periods of high ambient temperature and humidity. Typical patients are athletes and military recruits in basic training. In vitro muscle fiber testing reveals evidence of susceptibility to malignant hyperthermia in some patients who present in this fashion [12,13]. Exertional heat stroke is discussed in detail separately. (See "Exertional heat illness in adolescents and adults: Epidemiology, thermoregulation, risk factors, and diagnosis" and "Exertional heat illness in adolescents and adults: Management and prevention".)

In addition to an elevated core body temperature, common vital sign abnormalities in heat stroke include sinus tachycardia, tachypnea, a widened pulse pressure, and hypotension [14]. Note that the temperature reading of some patients with heat stroke may not exceed 40ºC, particularly if cooling measures were initiated prior to the patient's arrival at the hospital. In addition, some standard thermometers have a maximum reading below the temperatures sometimes reached by patients suffering from heat stroke, and thus give inaccurate and misleading information. A thermometer (rectal or esophageal) that is accurate at high temperatures must be used when assessing heat stroke patients.

If they can respond coherently, patients with heat stroke may complain of weakness, lethargy, nausea, or dizziness. The presentation of elder adults with heat stroke may be subtle and nonspecific early in the course of the disease.

Other physical findings may include flushing (cutaneous vasodilation), tachypnea, crackles due to noncardiogenic pulmonary edema, excessive bleeding, and evidence of neurologic dysfunction, such as altered mentation, slurred speech, irritability, inappropriate behavior, agitation, ataxia and other signs of poor coordination, delirium, seizures, and coma [15]. The skin may be moist or dry, depending upon underlying medical conditions, the speed with which the heat stroke developed, and hydration status [14]. Not all victims of heat stroke are volume-depleted [16].

Frequently encountered complications include acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), acute kidney injury (ie, acute renal failure), hepatic injury, hypoglycemia, rhabdomyolysis, and seizures [2,14]. (See 'Complications' below.)

RISK FACTORS

Factors associated with increased mortality — Patients who present to the hospital with heat stroke have high mortality, with rates ranging from 21 to 63 percent [17-19]. Mortality correlates with the degree of temperature elevation, time to initiation of cooling measures, and the number of organ systems affected [20]. According to one prospective cohort study, the risk of death increases substantially in patients who present with anuria (hazard ratio [HR] 5.24; 95% CI 2.29-12.03), coma (HR 2.95; 95% CI 1.26-6.91), or cardiovascular failure (HR 2.43; 95% CI 1.14-5.17) [18]. Patients who take long-term antihypertensive medications, lack access to air conditioning, or are socially isolated or unable to care for themselves are also at high risk [18,21-23].

Factors associated with increased risk — Important risk factors for the development of nonexertional heat stroke include extremes of age, dehydration, obesity, poor physical condition, lack of acclimatization, lack of air-

conditioning, and social isolation. Other risk factors include diabetes, cardiovascular disease, alcohol abuse, and a number of drugs. These include diuretics, medications with anticholinergic properties, sympathomimetics, salicylates, and the anti-epileptics topiramate and zonisamide [24].

DIAGNOSIS — The diagnosis of classic (nonexertional) heat stroke is made clinically based upon an elevated core body temperature (generally >40ºC [104ºF]), central nervous system dysfunction (eg, altered mental status), and exposure to severe environmental heat [2]. Patients with classic heat stroke generally have increased susceptibility to the heat due to age or underlying medical conditions, manifest characteristic examination findings, and lack another explanation for their hyperthermia (eg, infection). In addition to an elevated core body temperature, common examination findings in classic heat stroke include vital sign abnormalities (eg, tachycardia, tachypnea, hypotension), flushing, pulmonary crackles, oliguria, and neurologic abnormalities.

DIAGNOSTIC EVALUATION — A rectal temperature should be obtained in all patients suspected of heat stroke. Some standard thermometers have a maximum reading below the temperatures sometimes reached by patients suffering from heat stroke, and thus may give inaccurate and misleading information. A thermometer (rectal or esophageal) that is accurate at high temperatures must be used to assess and monitor heat stroke patients.

A chest radiograph should be obtained and may demonstrate pulmonary edema. The electrocardiogram may reveal dysrhythmias, conduction disturbances, nonspecific ST-T wave changes, or heat-related myocardial ischemia or infarction [25-27]. Laboratory studies may reveal coagulopathy, acute kidney injury (acute renal failure), acute hepatic necrosis, and a leukocytosis as high as 30,000 to 40,000/mm³ [1,2].

Laboratory studies to obtain in the patient with nonexertional heat stroke include:

- Complete blood count, basic serum electrolyte concentrations, blood urea nitrogen (BUN) and creatinine concentrations, and hepatic transaminase concentrations. Transaminase concentrations are rarely normal in patients with heat stroke; however, in patients with severe liver injury marked elevations may not appear for 24 to 48 hours [20,28-30].

- Prothrombin time (PT) and partial thromboplastin time (PTT), because of the risk of heat-induced liver damage and disseminated intravascular coagulation [31]. (See "Clinical features, diagnosis, and treatment of disseminated intravascular coagulation in adults".)

- Arterial or venous blood gas – Metabolic acidosis and respiratory alkalosis are the most common abnormalities [32]. (See "Simple and mixed acid-base disorders".)

- Studies to detect rhabdomyolysis (eg, serum creatine kinase, urine myoglobin) and its complications (eg, hypocalcemia, hyperphosphatemia, myoglobinuria, and BUN and creatinine) [33]. Myoglobinuria should be suspected in any patient with brown urine supernatant that is heme-positive and clear plasma. Urinalysis may reveal other evidence of renal injury, including protein, blood, renal tubular casts, and increased specific gravity [34]. (See "Clinical manifestations and diagnosis of rhabdomyolysis" and "Clinical features and diagnosis of heme pigment-induced acute kidney injury".)

- Toxicologic screening may be indicated if a medication effect is suspected. Drugs that may contribute to hyperthermia and for which tests are often available include ethanol, amphetamines, cocaine, salicylates, hallucinogens, and lithium. (See "General approach to drug poisoning in adults" and "Initial management of the critically ill adult with an unknown overdose".)

- A head CT and analysis of the cerebrospinal fluid should be performed as indicated if central nervous system causes of altered mental status are suspected [14].

DIFFERENTIAL DIAGNOSIS — The differential diagnosis of severe hyperthermia is extensive and includes infectious, endocrine, central nervous system, toxic, and oncologic etiologies (table 1).

Nonexertional (classic) heat stroke can often be distinguished from other conditions based solely upon the history and physical examination, particularly in at-risk patients during a heat wave. However, the clinical picture can be unclear. As examples, an elderly woman found unconscious in a sealed house in the middle of summer who has a core temperature of 41.2ºC (106.2ºF) presents many more diagnostic possibilities than a college football player who collapses during summer practice and has the same temperature. The woman may be suffering from sepsis,

cerebral hemorrhage, anticholinergic toxicity, withdrawal from a central nervous system depressant, or a host of other conditions. Conversely, her elevated temperature may be due solely to heat exposure.

No single diagnostic test definitively confirms or excludes heat stroke. Furthermore, laboratory study abnormalities may overlap in patients with heat stroke and with hyperthermia due to other conditions. As an example, patients with heat stroke frequently meet criteria for the systemic inflammatory response syndrome (SIRS) [35]. It may be impossible early in the patient's course to distinguish the two conditions. In such cases when the etiology of hyperthermia is unclear but heat stroke remains a possibility, it is prudent to initiate cooling measures while diagnoses other than heat stroke are pursued.

Rapid improvement with active cooling suggests that heat stroke is the primary diagnosis. However, improvement may not occur or may occur gradually, particularly in older debilitated patients, depending upon the degree and duration of hyperthermia and other factors. As an example, patients with compromised cardiovascular function due to underlying disease (eg, heart failure) or medications (eg, beta or calcium channel blocker) have limited capacity to respond to increased environmental heat and humidity [36]. In patients whose mental status remains depressed despite effective cooling measures, clinicians should investigate alternative causes for hyperthermia, including conditions affecting the central nervous system (eg, meningitis, cerebral hemorrhage, hypothalamic stroke). Brain imaging and analysis of cerebrospinal fluid may be necessary.

The most important causes of severe hyperthermia (greater than 40ºC [104ºF]) due to a failure of thermoregulation are heat stroke, neuroleptic malignant syndrome, and malignant hyperthermia. The context in which symptoms develop usually suggests the etiology (eg, exertional heat stroke following exercise in high ambient temperature and humidity; malignant hyperthermia after anesthetic agents; neuroleptic malignant syndrome (NMS) among patients treated with antipsychotic medications). Each of these conditions may be associated with severe systemic complications and death. The types of heat stroke are defined below. (See 'Definitions and clinical findings' above.)

Malignant hyperthermia is a rare autosomal dominant disorder that manifests following treatment with anesthetic agents, most commonly succinylcholine and halothane. The onset of malignant hyperthermia is usually within one hour of the administration of general anesthesia, but rarely may be delayed up to 10 hours after induction. Early clinical findings include muscle rigidity (especially masseter stiffness), sinus tachycardia, hypercarbia, and skin cyanosis with mottling. Marked hyperthermia (up to 45ºC [113ºF]) occurs minutes to hours later. (See "Malignant hyperthermia: Clinical diagnosis and management of acute crisis".)

Neuroleptic malignant syndrome is an idiosyncratic reaction most frequently associated with first- and second-generation antipsychotic agents. In addition to hyperthermia, NMS is also characterized by "lead pipe" muscle rigidity, altered mental status, choreoathetosis, tremors, and evidence of autonomic dysfunction, such as diaphoresis, labile blood pressure, and dysrhythmias. (See "Neuroleptic malignant syndrome".)

MANAGEMENT

Initial treatment and monitoring — The management of nonexertional (classic) heat stroke requires ensuring adequate airway protection, breathing, and circulation; rapid cooling; and treatment of complications. The management of exertional heat stroke is discussed separately. (See "Exertional heat illness in adolescents and adults: Management and prevention".)

Tracheal intubation and mechanical ventilation are needed for patients unable to protect their airway or with deteriorating respiratory function. (See "Rapid sequence intubation for adults outside the operating room" and "Mechanical ventilation of adults in the emergency department".)

Central venous pressure (CVP) monitoring may be useful for assessing volume status and determining the need for fluid resuscitation [16]. A target CVP of 8 to 12 mmHg is an appropriate target. However, CVP readings may be inaccurate if heat-related cardiac dysfunction develops (eg, acute right heart failure). Alpha-adrenergic agonists should be avoided, since the resultant vasoconstriction decreases heat dissipation. Instead, hypotension or volume depletion is treated with discrete intravenous (IV) boluses of isotonic crystalloid (eg, isotonic saline in boluses of 250 to 500 mL).

Continuous core temperature monitoring with a rectal or esophageal probe is mandatory, and cooling measures should be stopped once a temperature of 38 to 39ºC (100.4 to 102.2ºF) has been achieved in order to reduce the risk of iatrogenic hypothermia [14].

Cooling measures — Evaporative and convective cooling is the method used most often to treat classic heat stroke because it is effective, noninvasive, easily performed, and does not interfere with other aspects of patient care. When used to treat elderly patients with classic heat stroke, evaporative and convective cooling is associated with decreased morbidity and mortality [4,37,38].

With evaporative and convective cooling, the naked patient is sprayed with a mist of lukewarm water while fans are used to blow air over the moist skin. Special beds called body cooling units have been made for this purpose [4]. Agitation from an altered mental status or shivering induced by evaporative and convective cooling or other treatments may generate heat and can be suppressed with short-acting IV benzodiazepines, such as lorazepam (1 to 2 mg IV). Benzodiazepines may also improve core body cooling [39]. If neuroleptic malignant syndrome (NMS) is **not** suspected and benzodiazepines are ineffective at controlling shivering, chlorpromazine (25 to 50 mg IV) may be used. However, chlorpromazine has anticholinergic properties and thus, may impair sweating and exacerbate hypotension. (See "Neuroleptic malignant syndrome".)

Other effective cooling methods are less commonly used in patients with classic heat stroke. Immersing the patient in ice water (cold water immersion) is an efficient, noninvasive method of rapid cooling [40], but it complicates monitoring and intravenous access, and may be harmful to elder patients [4]. An alternative method that allows greater access to the patient is water ice therapy (WIT), in which the patient is placed supine on a porous stretcher positioned on top of a tub of ice water. Medical personnel continuously pour ice water from the bath onto the patient and massage major muscle groups with ice packs to increase skin vasodilation [41]. Applying ice packs to the axillae, neck, and groin (areas adjacent to major blood vessels) is another effective cooling technique, but may be poorly tolerated by the awake patient. A small randomized trial, in healthy subjects with exercise-induced hyperthermia, reported that applying cold compresses to the glabrous (smooth, hairless) skin surfaces of the cheeks, palms, and soles led to more rapid cooling than applying them to the axillae, neck, and groin [42]. This approach warrants further study in classic heat stroke patients with comorbidities that might impair peripheral vasodilatation.

Cold thoracic and peritoneal lavage results in rapid cooling. However, it is invasive and peritoneal lavage is contraindicated in pregnant patients and those with previous abdominal surgery. Cooled oxygen, cooling blankets, and cold (ie, room temperature, or approximately 22°C [71.6°F]) intravenous fluids may be helpful adjuncts. Cold gastric lavage may cause water intoxication [2].

Recommendations for the treatment of heat stroke are based primarily upon small observational studies. A systematic review of clinical studies investigating the treatment of heat stroke noted the following [4]:

- There are no definitive studies supporting any particular approach to cooling in classic heat stroke.
- Evaporative and convective cooling methods for the treatment of classic heat stroke are better tolerated.
- Immersion in ice water is rapid and effective in young patients with exertional heat stroke. However, immersion therapy is associated with increased mortality when used to treat elderly patients with classic heat stroke.
- Pharmacologic therapy (eg, dantrolene) is ineffective and **not** indicated in the treatment of exertional or classic heat stroke.

Alcohol sponge baths should be avoided because large amounts of the drug may be absorbed through dilated cutaneous vessels and produce toxicity [1].

Pharmacologic therapy — Pharmacologic therapy is not required in heat stroke. There is no role for antipyretic agents such as acetaminophen or aspirin in the management of heat stroke, since the underlying mechanism does not involve a change in the hypothalamic set-point and these medications may exacerbate complications such as hepatic injury or disseminated intravascular coagulation (DIC) [14]. Salicylates can contribute to hyperthermia by uncoupling oxidative phosphorylation. Dantrolene is ineffective in patients with severe temperature elevation **not** caused by malignant hyperthermia [43,44]. In cases where the etiology of the patient's

hyperthermia is unclear initially and infection remains a possibility, empiric administration of an initial dose of antibiotics, following collection of appropriate cultures, is prudent, while cooling measures are implemented.

Complications — Severe nonexertional hyperthermia may lead to a wide range of complications. These often resolve as cooling measures take effect, but this depends upon the degree and duration of hyperthermia. Complications may include the following:

- Respiratory dysfunction – Patients with nonexertional heat stroke often develop pulmonary complications, which can include aspiration, bronchospasm, noncardiogenic pulmonary edema, acute respiratory distress syndrome, pneumonitis, pulmonary infarction, and pulmonary hemorrhage. Tracheal intubation and mechanical ventilation are often necessary to protect the airway and to address increased metabolic demands (ie, provide supplemental oxygen and increased minute ventilation). In a review of 28 patients admitted with heat stroke, 24 (86 percent) developed respiratory failure with most requiring mechanical ventilation [29]. (See "Advanced emergency airway management in adults" and "Rapid sequence intubation for adults outside the operating room" and "Acute respiratory distress syndrome: Supportive care and oxygenation in adults" and "Mechanical ventilation of adults in acute respiratory distress syndrome".)

- Arrhythmia and cardiac dysfunction – Potential cardiac complications include acute decompensated heart failure and myocardial injury associated with reversible cardiac biomarker increase and ST-segment changes on electrocardiogram (ECG). The biomarker and ECG changes are believed to be caused by an increase in catecholamine levels due to heat stroke, causing a stress-induced cardiomyopathy [45,46]. Other ECG abnormalities that have been reported in association with heat stroke include sinus tachycardia and other tachyarrhythmias, conduction abnormalities, prolonged QT interval, transient Brugada pattern, and nonspecific ST-T changes [26,47]. Rapid cooling is essential; cardiac dysfunction and tachyarrhythmias generally resolve with cooling. Antiarrhythmics are seldom necessary and electrical cardioversion should be avoided until cooling is achieved, unless necessary to treat ventricular fibrillation or pulseless ventricular tachycardia.

- Hypotension – Hypotension associated with heat stroke results from peripheral vasodilation, cardiac dysfunction, and volume depletion. Treatment consists primarily of discrete intravenous (IV) boluses of isotonic crystalloid (eg, isotonic saline 250 to 500 mL). Given the risk of pulmonary edema, excessive fluid administration should be avoided. Alpha-adrenergic agonists cause vasoconstriction, which impairs cooling, and these should be avoided if possible.

- Seizures – Seizures are common in patients with heat stroke. Initial treatment consists of short-acting benzodiazepines, while cooling measures are initiated. Midazolam 0.1 to 0.2 mg/kg IV, to a maximum dose of 4 mg, has an onset of action one to five minutes and duration of action of one to six hours. Lorazepam 0.1 mg/kg IV, to maximum dose of 4 mg, is a second-line option, as the duration of action may be prolonged from 12 to 24 hours. Barbiturates should be avoided. Rapid cooling is essential to treatment. (See "Convulsive status epilepticus in adults: Treatment and prognosis", section on 'Benzodiazepines'.)

- Rhabdomyolysis – The combination of muscle injury, volume depletion, and acute kidney injury can lead to rhabdomyolysis in patients with heat stroke. Standard therapies are used for treatment and these are discussed separately. (See "Clinical features and diagnosis of heme pigment-induced acute kidney injury".)

- Acute kidney injury – Heat stroke can cause acute kidney injury. Renal function studies and serum electrolyte concentrations should be followed closely over the first few days of illness; renal replacement therapy may be needed [20].

- Hepatic injury – Hepatic injury due to heat stroke is generally self-limited but in some cases may progress to acute liver failure, with a subset of patients requiring liver transplantation [48].

- Disseminated intravascular coagulation (DIC) – DIC can develop during the first three days of illness and coagulation studies should be monitored during this period. Replacement of clotting factors with fresh frozen plasma and platelets may be necessary. (See "Clinical features, diagnosis, and treatment of disseminated intravascular coagulation in adults".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade

reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Heat stroke (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Body temperature is maintained within a narrow range by balancing heat load with heat dissipation. Evaporation is the principal mechanism of heat loss in a hot environment, but becomes ineffective above a relative humidity of 75 percent. The other major methods of heat dissipation, including conduction and convection, cannot efficiently transfer heat when environmental temperature exceeds skin temperature. (See 'Pathophysiology' above.)

- The differential diagnosis of hyperthermia is extensive and includes infectious, endocrine, central nervous system, and toxic etiologies (table 1). The most important causes of severe hyperthermia (greater than 40ºC [or 104ºF]) caused by a failure of thermoregulation are heat stroke, neuroleptic malignant syndrome, and malignant hyperthermia. (See "Neuroleptic malignant syndrome" and "Malignant hyperthermia: Clinical diagnosis and management of acute crisis".)

- Severe nonexertional hyperthermia (classic heat stroke) carries a high mortality rate. Mortality correlates with the degree of temperature elevation, time to initiation of cooling measures, and the number of organ systems affected. (See 'Risk factors' above.)

- The diagnosis of nonexertional heat stroke is made clinically based upon an elevated core body temperature (generally >40°C), central nervous system dysfunction (eg, altered mental status), exposure to severe environmental heat, and the absence of another explanation for hyperthermia. Patients with classic heat stroke generally have increased susceptibility to the heat due to age or underlying medical conditions. Diagnostic studies are generally nonspecific but may reflect cardiovascular, renal, or hepatic dysfunction, or coagulopathy. Studies to be obtained are described in the text. (See 'Definitions and clinical findings' above and 'Diagnosis' above and 'Diagnostic evaluation' above.)

- The management of nonexertional heat stroke consists of ensuring adequate airway protection, breathing, and circulation; rapid cooling; and treatment of complications. Tracheal intubation and mechanical ventilation are often necessary. Hypotension or volume depletion is treated with discrete intravenous boluses of isotonic crystalloid; alpha-adrenergic agonists should be avoided if possible. (See 'Management' above.)

- We suggest that rapid cooling of patients with nonexertional heat stroke be performed using evaporative and convective techniques (**Grade 2C**). Evaporative and convective cooling techniques are safe and effective in nonexertional heat stroke and do not interfere with patient access or monitoring, or other treatments. Cold water immersion may be harmful to elder patients; there is no role for antipyretic agents. Continuous core temperature monitoring with a rectal or esophageal probe is mandatory in all patients being treated for heat stroke. The management of exertional heat stroke is discussed separately. (See 'Cooling measures' above and "Exertional heat illness in adolescents and adults: Management and prevention".)

- Nonexertional heat stroke can cause a number of complications, including respiratory and cardiac dysfunction, hypotension, seizures, rhabdomyolysis, acute renal and hepatic injury, and disseminated intravascular coagulation. (See 'Complications' above.)

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GRAPHICS

Differential diagnosis of hyperthermia*

Infection	Drug or toxin related	Neurologic	Environmental	Endocrine	Oncologic
Sepsis	Malignant hyperthermia	Hypothalamic stroke	High temperature and humidity	Thyroid storm	Lymphoma
Meningitis	Neuroleptic malignant syndrome	Status epilepticus		Pheochromocytoma	Leukemia
Encephalitis	Withdrawal syndromes (eg, alcohol, sedative hypnotic)	Cerebral hemorrhage		Diabetic ketoacidosis	
Brain abscess	Cocaine				
Tetanus	Sympathomimetic poisoning (eg, amphetamines)				
Typhoid fever	Anticholinergic poisoning (eg, antihistamine)				
Malaria	Serotonin syndrome				
	Stimulant-containing dietary drugs				
	Salicylate poisoning				

*While cardiovascular disease does not directly cause heat illness, compromised cardiovascular function from underlying disease (eg, heart failure) or medication (eg, beta or calcium channel blocker) impairs a patient's ability to respond to increased environmental heat and humidity, and can contribute to heat illness.

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